AN EVALUATION OF KETAMINE HYDROCHLORIDE FOR USE IN PEDODONTIC OUT-PATIENTS

By

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CURRICULUM VITAE

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INTRODUCTION

A new anesthetic, ketamine hydrochloride,[a] has recently received considerable attention in the medical profession for use in short surgical and diagnostic procedures. Ketamine is described by the manufacturer as a non-barbiturate anesthetic formulated as a slightly acidic (pH 3.5 - 5.5) solution and available in concentrations of 10, 50 or 100 mg per milliliter.[1] Among this agent's unique properties are the following: selective depression of the higher centers of the brain without adversely affecting cardiac and respiratory centers, maintenance of protective pharyngeal and laryngeal reflexes, and rapid and profound anesthesia. The drug is administered either intravenously or intramuscularly and can be used safely without intubation.

Since its first clinical trials less than ten years ago, ketamine has been used in minor surgery, obstetrics, ophthalmology, cardiac catheterizations, orthopedics, and burn patients. The results of these early clinical trials suggest promise for the use of ketamine in other applications but they also point out these undesirable side effects: long recovery time, unpleasant postoperative physic reactions, and nausea.

A safe, effective anesthetic agent is urgently needed for pedodontic patients who pose severe behavior management problems. At present, medium to high doses of narcotics or barbiturates are most commonly used to sedate these patients. However, high doses of these drugs pose the threat of respiratory and cardiac depression. Consequently, for the patient's safety, it is sometimes necessary to admit an unmanageable child to the hospital for a conventional gaseous, general anesthetic. Although it may be indicated, a hospital admission

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[a]Ketalar, Park-Davis and Company, Detroit, Michigan. Figure 1.

can represent a large expense to the family and a loss in productive time for the dentist.

If the dentist chooses to treat the child as an out-patient with local anesthetic plus subanesthetic doses of a central nervous system depressant, he may choose one of the following:[2]

> (1) Psychosedatives: diazapam (Valium®), hydroxyzine (Atarax®), phenothiazines; (2) Narcotics: meperidine (Demerol®); (3) Belladonna derivates: atropine, scopolamine; (4) Barbiturates: secobarbital (Seconal®), amobarbital (Tuinal®); (5) Nitrous oxide analgesia.

Even under the best circumstances, it is difficult to determine the appropriate dose for a particular patient to produce a sedative effect without the inherent danger of central nervous system (CNS) depression. When the child is in an acute state of anxiety, a large sedative dose with any one or combination of the above agents can be hazardous.

It is most desirable if a drug can be employed which will produce profound anesthesia with a minimal dose and still satisfy as many of the following criteria as possible.[2]

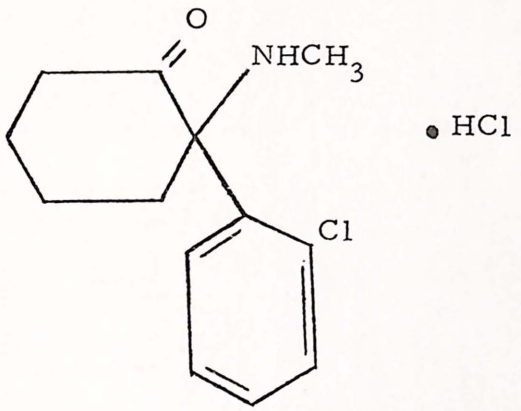
> (1) Effective analgesia or pain control, (2) partial or complete amnesia, (3) patient cooperation, (4) an accessible, dry operative field, (5) minimal impairment of the operative field, (6) comfortable positioning of the patient, dentist, and anesthetist, and (7) complete safety.

The hypothesis of this study is that by reducing the total amount of ketamine that is administered for the anesthesia period, undesirable side effects may be reduced, including nausea, post emergence psychic reactions and prolonged recovery time. Droperidol and nitrous

oxide-oxygen with psychosedative and analgesic properties may be effective in combination with ketamine to prolong working anesthesia time while reducing these other undesirable side effects.

This investigation had four principal objectives in the evaluation of ketamine for pedodontic out-patient care. The first concern was to determine if small doses of ketamine would produce satisfactory anesthesia for sufficient periods to complete dental procedures. Secondly, the recovery period was measured, as its length is an important factor in out-patient care. A third objective was to compare a series of patients anesthetized by a mixture of ketamine and scopalamine with this mixture combined with droperidol and this mixture associated with nitrous oxide-oxygen. Finally the incidence of complications, side effects, and unfavorable operator or parent responses was also assessed.

The following is a summary of the chemical structure, dosage, and commercially available preparations of ketamine. Ketamine



hydrochloride[1] [dl 2-(o-chlorophenyl)-2-(methylamino) cyclohexanone hydrochloride] is available commercially in dosages of 10, 50, or 100 mg per ml. It contains 0.1 mg/ml Phemerol® (benzethonium chloride) as a preservative. The average recommended dosages to produce surgical anesthesia are 1 mg/lb IV and 3-6 mg/lb IM.

REVIEW OF LITERATURE

Development and Pharmacology of Ketamine

Ketamine Hydrochloride is a member of the arylcycloalklamines, a class of centrally acting anesthetic drugs. The first general anesthetic agent in this family, phencyclidine, was discovered over fifteen years ago. Phencyclidine research was abandoned when another member of this class of drugs, ketamine, was shown to have fewer side effects.[3]

To determine toxic proportions of ketamine, acute toxicity determinations were carried out in rodents and rhesus monkeys by Kaump et al.[4] Using varying schedules of administration and frequency, dosages were increased and the number of surviving animals was recorded until toxic levels were reached. Young and old animals were used to add another physical variable in the use of the drug. Kaump conducted laboratory studies of blood, bone marrow, and serum chemistry in both toxic and subtoxic dose states. Autopsy and histological evaluations for drug-related changes in body tissues were also performed.

The acute toxicity studies were conducted by giving mice and rats increasing dosages of ketamine injected intraperitoneally until 50 per cent or more of the test animals expired. Most deaths, Kaump and associates[4] reported, occurred within two hours of the injection. They stated:

> There was initial excitement and irritability, rapidly followed by depression, severe incoordination, and prostration. Recovery followed in reverse sequence... Complete autopsy examination of a number of rats surviving treatment at, or greater than, the LD_{50} values revealed no evidence of organ damage.

In Kaump's study the intraperitoneal LD_{50} doses ranged from 229 to 275.4 mg/kg in mice and 146.2 to 248 mg/kg in rats depending on age. Although the exact number of test animals is not mentioned, the project apparently contained a large sample and the above figures represent a good approximation of lethal dosages in these animals. In the same study, rodents given ketamine in light to medium dosages daily for six weeks showed minor changes in laboratory values, but no drug-related gross or microscopic organ damage was noted. Kaump also found that after injecting large dosages of ketamine in dogs intramuscularly during a period of five days, the righting reflex returned in 33 to 54 minutes and hematologic, urine and bone marrow values remained normal. Serum chemistry values were also within normal limits, except for elevated transaminase values. Kaump hypothesized that this increase was related to local muscle injury at the site of injection. In other trials a pair of dogs were given successively higher doses up to 160 mg/kg. After the dogs were sacrificed, examination showed slight elevation in blood alkaline phosphatase and transaminase values but no apparent evidence of organ damage.

Kaump used an unspecified number of rhesus monkeys in trials introducing ketamine intravenously for 1-6 hours in duration in 8 or 12 doses over a period of 28 or 41 days. There was a slight overall decrease in respiration, heart rate, blood pressure, and body temperature. The blood changes were minor with some unspecified incidences of leukocytosis, neutrocytosis, and sedimentation increases. Test animals showed a return to normal values in 7 to 21 days. Within the limitations of the study sample, this animal investigation is probably adequate to demonstrate that very high dosages of ketamine are needed to produce lethal effects. Even repeated, high, subtoxic dosages failed to produce lasting, observable harmful effects clinically or histologically in the animals studied.

Chen[5] used several different animal species, varied the dosage of ketamine and observed changes in behavioral, electroencephalograph (EEG), and cardiovascular values. Initially he noted a characteristic behavior, catalepsy, in his animals anesthetized with ketamine in light dosages. Catalepsy is a trance-like state of consciousness in which the limbs are rigid and retain any position in which they are placed. Chen compared the responses of some of his test animals to both ketamine and sodium thiamylal, a short acting barbiturate. With the barbiturate, catalepsy occurred only during emergence from the anesthetic. Using EEG recordings, the barbiturate produced a relaxed, depressed range of activity, whereas the arylcycloalkylamine elicited both a slow and excited range of values. No tolerance to repeated administration of ketamine was demonstrated as was observed with sodium thiamylal.

As dosages approached lethal levels with ketamine, Chen reported convulsions in some animals. Barbiturate anesthetics do not produce this effect. In the rhesus monkey catalepsy under ketamine begins in the lower limbs and then proceeds to the upper regions, whereas recovery begins in the upper limbs and proceeds downward. The rhesus monkey during recovery was alert and able to turn its head well before it was able to direct its lower limbs. Chen pointed out that the undesirable psychic effects of the arylcycloalkylamines in human subjects occur during emergence when the subject is beginning to perceive disturbed motor and sensory input and feels a sense of being incapacitated. Barbiturates at least provide a degree of hypnosis during the emergence period which can mask these disturbing perceptions.

In larger studies with electrodes implanted in the brains of cats, Corssen et al[6] and Winters et al[7] described contrasting EEG effects during ketamine anesthesia at various levels of the brain. Corssen

found changes in EEG values in the neocortex and subcortical structures, such as the thalamus, suggesting that the main action of the drug is here. However, the limbic system in the hippocampus demonstrates increased excitation. Corssen considered that the changes in the higher centers of the brain indicate a depressive effect, whereas he described the changes in the hippocampus as excitatory. For these drug-related changes in the two regions, he has popularized the term "dissociative." This concept describes a response in which higher centers of the brain appear depressed and certain association pathways are interrupted.

Corrsen et al stimulated the median nerves in test animals anesthetized with ketamine and measured potentials reaching the somatosensory areas of the cortex. They demonstrated that ketamine significantly reduced the somatosensory impulses reaching the cortex, but not the midbrain, significantly more than the controls. As Corssen pointed out, barbiturates suppress midbrain activity even in low dosages.

Winters has expressed concern about increased EEG activity in the hippocompus in cat and human subjects during ketamine anesthesia. He compared these EEG recordings to those seen during epileptic seizures. He did not, however, state that ketamine causes actual seizures even in epileptics. In fact, Winters described two epileptic human subjects who demonstrated seizure activity in the hippocampus on EEG recordings but failed to show behavioral signs of any seizures. However, after analyzing his results, one would be reluctant to use ketamine in an epileptic patient with a history of uncontrolled grand mal seizures.

Winters' study illustrates the principle that general anesthesia can be induced by an agent which either depresses or excites the central nervous system and therefore renders the subject unresponsive to outside pain stimuli. In his investigation, Winters placed 16 cats

with chronically implanted brain electrodes in a surgical plane of anesthesia using ketamine. After evaluating behavioral and EEG data, he concluded that ketamine is a CNS excitatory agent which renders the subject unresponsive to outside stimuli.

In a similar study using a cat and a baboon monkey, Szappanyos and associates[8] confirmed the findings of Corssen and Winters in that the thalmo-cortical system showed increased spike and wave activity on the EEG. Moreover, using electrodes implanted in the dura mater, he detected an increase in the electrochemical response to visual and acoustic stimulations. Also the increased extracortical activities on the EEG tracings remained visible for an unspecified time after the drug had worn off.

Conducting in vivo experiments in dogs, Szappanyos measured cardiovascular response during IV injections of ketamine in usual anesthetic dosages. A depressor-like effect was detected initially in cardiac output, blood pressure, peripheral vascular resistance, and heart rate. These responses were followed in less than one minute by a pressor effect. No indication of any arrythmias was noted on the EEG tracing even during injection of ketamine.

Ketamine produces profound anesthesia by both the IM and IV routes of administration. However, as we shall see in clinical studies, the IM route requires approximately five times the average dosage to produce surgical anesthesia.[9, 10, 11, 12] In a study performed in rats, Chang[13] determined that the plasma has a smaller binding capacity and greater dissociation rate than muscle tissue. He concluded that the intravenous route would be the first choice and intramuscular the next best route of administration. In the same study, the tissue concentrations in an anesthetized animal were found to be 10 times those found in the plasma. Chang theorized that it would require a 10 times greater dose to saturate body fat before the drug would diffuse into the plasma;

therefore the operator should avoid placing an injection of ketamine in subcutaneous fat tissue.

Clinical Trials of Ketamine in Human Subjects

Although the intravenous method offers more rapid, carefully controlled administration of ketamine, intramuscular injection is often more feasible for burn patients, small children, infants, or behavior problem patients.[14, 15, 16] Induction of anesthesia usually occurs in 30-40 seconds by the intravenous route and 3-7 minutes when given intramuscularly.[9, 14, 17] Nystagmus is commonly observed initially when the eyes are open and ceases after several minutes.[11, 18] The eyelid reflex usually remains, but some patients close their eyes and appear to be in a deep state of anesthesia.[17, 19, 20] Muscle tone remains and some involuntary purposeless movements are seen.[2, 6] Patients are able to swallow their own fluids.[20] Vocalization may occur even during periods when the subject is anesthetized deeply enough for the procedure.[17, 21] Laryngeal and pharyngeal reflexes have been observed to be within normal limits.[18, 19]

Most observers in early clinical studies report an initial increase in blood pressure and heart rate for the first 15-20 minutes.[2, 8, 9, 14, 16, 17, 22, 23] Blood pressure increases and tachycardia averaged 8.1 per cent and 4.3 per cent, respectively, in one report of over 1500 anesthetic cases. The intramuscular route of administration demonstrated reduced cardiac changes compared to the intravenous means.[24] No arrhythmias have been reported[13, 25, 26, 27] and one observer stated that ketamine has "antiarrhythmic effects."[23]

Ketamine reportedly produces only mild effects on respiration, usually consisting of a mild and transient depression during or soon after administration.[2, 6, 9, 28] Again these effects are much more likely to occur after rapid intravenous induction than by the

intramuscular route. Ketamine apparently does not have a direct depressant effect on the respiratory center or secondarily on other respiratory reflexes.[5, 9, 28] Therefore, within therapeutic dosage ranges, respiratory depression or sustained apnea has been reported not to occur.[18, 19] Observers indicate that an orotracheal airway or respiratory assistance is unnecessary and that the patient is able to maintain adequate spontaneous respiration by breathing room air.[20, 28] However, in a large study involving over 1500 surgical procedures, inadequate respiration resulting from excessive salivation or mechanical obstruction during ketamine anesthesia was reported for 2.6 per cent of the cases.[9] Overdoses causing central depression (1.3 per cent) and laryngobronchospasm (0.4 percent) caused other incidents in which respiratory assistance was rendered to the patient. Morgan[17] reported the highest incidence of mechanical airway obstruction (11.5 percent). In this study, however, the anesthetist was able to correct the blockage by adjusting the patient's head or by using an oropharyngeal airway. In another report using ketamine, Brueggemann and Helveston[26] observed one airway obstruction in 44 patients. This obstruction occurred in a child with Down's syndrome. The anesthetist thought it necessary to intubate the patient and continue with a gaseous anesthetic.

Immediately after administration of ketamine, most observers report a generalized increase in muscle tone throughout the body. Such conditions may contraindicate thoracic or abdominal surgery but cause few problems for more superficial procedures.[14, 29] Oral surgeons report the need to maintain the mouth open by mechanical aids.[6, 18] Purposeless body movements are also seen commonly during some part of a procedure using ketamine.[2, 14, 28] Usually these movements occur as the subject is beginning to emerge or has been given an insufficient dose.[6, 10, 12] Although these movements

are generally not enough to warrant concern, ketamine is considered unsatisfactory by some authors for orthopedic and eye surgery or other deep or long-term surgical procedures where absolute immobility is essential.[21, 26]

One of the interesting side effects observed by clinical investigators was a certain incidence of psychic reactions by the patient during emergence. As discussed previously, studies by Chen[5] and Winters[7] described enhanced activity in the central nervous system as recorded by EEG tracings. Unlike other general anesthetics which provide a sedative or hypnotic effect during recovery, ketamine causes a greater amplitude of sensory input.

Clinically, many observers report a varying incidence of vivid dreaming or in some cases hallucinations by subjects during emergence.[22, 30] These dreams may be pleasant or unpleasant. During this period the subject may vocalize or move, indicating a phase of vivid dreaming. In one study of 138 anesthetic cases, with patients aged from 2 months to 89 years, 33 per cent could not recall what the dreams were about.[17] Twenty patients stated that they had experienced pleasant dreams; however, 10 per cent of the patients in this study recalled "vivid, frightening dreams" and indicated that they would not undergo anesthesia with the same agent again. Morgan[17] pointed out that of the 32 children in this report under the age of 14, only one recalled dreaming and this dream was not frightening. The patients who described frightening experiences had been given IV administrations. The children were given the agent intramuscularly due to the greater ease of administration.

Corssen[9] emphasized the importance of not disturbing the patient during the recovery period. He maintained that the patient is still in a dissociated mental state and incapable of relating normally to his environment.

> Attempts to arouse the patient while he is still unable to see and hear and to orient himself may set in motion a chain of anxiety reactions which ultimately can lead to severe psychomotor outbreaks and irrational behavior.

Corssen stated that during recovery the patient should be shielded from any outside verbal, light, or tactile stimuli. Although this aspect was not an objective of his study, Corssen observed that most psychic disturbances were seen in adult patients and usually resulted when premature attempts were made to awaken them. After evaluating 1508 cases, he reported an overall incidence of 2.8 per cent of vivid dreaming and 0.20 per cent incidence of hallucinations.

Applications to Outpatient Dental Procedures

Ketamine HCl only recently began to be studied for its suitability for oral surgery and restorative dentistry. In an oral surgery study of 115 patients aged 1 to 58 years with an average age of 7 years, Corssen and Hayward administered ketamine IV in 112 procedures at 0.25-1 mg/lg and IM in 3 cases at 5 mg/lb.[6] No local anesthetics were employed. A transient respiratory depression was sometimes observed during rapid IV administration and increased salivary activity was reported. Increased secretions in the bronchial tree and in the oral cavity presented a danger of aspiration of fluids in the lungs and decreased gaseous exchange. Afterward an antisialagogue, scopolamine, was given IM 15-20 minutes before the ketamine. As in other reports,[18, 19, 31] Corssen confirmed the maintenance of protective swallowing reflexes and the fact that an orophryngeal or orotracheal airway was not needed. Although no vomiting was encountered during anesthesia, six patients vomited during the recovery period, perhaps due to the swallowing of blood.[6, 32]

In the same study, Corssen recorded the average time interval from the intravenous administration of ketamine until the patient could walk unaided. Using a dose of 1 mg/lb, the average recovery time was 42 minutes. Reducing the dosage to as little as 1/4 mg/lb IV did not significantly reduce the average recovery time. This is a remarkable and unexpected response and the authors were unable to account for these results.

Several studies have reported that the working time for the IV route (10-15 minutes) was far shorter than for the IM route (20-40 minutes).[6, 10, 12, 33] As might be expected, the recovery time for IV administration (40-60 minutes) was also much shorter than for IM (120-180 minutes).[6, 10, 12, 33] Using the IM route exclusively, Birkhan[18] demonstrated a longer average recovery time of 3-1/2 hours. However, he defined recovery more strictly as "full ambulation and orientation." Birkhan also reported a low incidence of vomiting (4%) of 25 cases and no unpleasant emergence reactions.

Another oral surgeon, Hellinger[19] used ketamine in a study of fifty adult patients because the respiratory and cardiovascular systems and the protective reflexes were maintained with this agent; however, due to a relatively high incidence of severe hallucinations (14%) and unpleasant vivid dreaming, he recommended limiting its use to patients with cardiovascular or respiratory disease. All studies mentioned here used similar recommended dosages of 1/2 -1 mg/lb IV and 4-6 mg/lb IM.

Two researchers attempted to use ketamine IM in smaller dosages, 0.5 - 1.5 mg/lb to obtain light anesthesia and analgesia and reduce the length of recovery time.[11, 33] Using ketamine, atropine, and local anesthetic, Shane[33] performed oral surgery and restorative dentistry on an unspecified number of children. The

report included only the clinical impressions of the author, who thought the lessened dosage was unsatisfactory to complete his procedures. Shane thought that although the patient might be able to hear quite well, he seemed unable to control his exaggerated muscular uncoordination. Shane described the subject as being still in a recovery-like state and being disturbed by the noise of the high speed and suction and the pressure of the biteblock and extractions.

On the other hand, in a more recent oral surgery study with 700 patients, Greenfield[11] combined small dosages of ketamine with nitrous oxide analgesia (with a limit of 50% nitrous oxide) and recorded satisfactory working time of 10-35 minutes, combined with a shortened recovery time of 5-30 minutes. Greenfield did not outline the criteria for recovery but described it as the point for discharging the patient. As no adverse psychic reactions or other complications were reported and the recovery time was effectively shortened, it appears that this method of administration should be explored as a very desirable method of anesthesia.

Agents Which May Supplement Ketamine Anesthesia

In several studies, droperidol[1, 16, 28, 34, 35, 36] has been suggested as a means to reduce unpleasant side effects of ketamine such as vomiting and psychic reactions. It has also been suggested that a combination of nitrous-oxide and ketamine, such as is used in medical surgical applications, might be useful in shortening the recovery time by making repeat injections of ketamine unnecessary.[9, 11, 37]

Droperidol[a] is a butyrophenone and is used as a powerful tranquilizer, an antiemetic, and an adreneric blocking agent. When it has been combined with ketamine, certain clinical observers have noted the absence of hallucinations and postoperative vomiting.[34, 35, 38] One observer suggested that the tachycardia effects of ketamine may

[a]Inapsine, McNeil Laboratories, Inc. Fort Washington, Pa. Figure 1.

be countered by the bradycardia effects of droperidol.[35]

Sadove et al[34] used sixty patients in a double blind study, giving droperidol preoperatively in three dosage ranges: 0.03 mg/lb, 0.06 mg/lb, and 0.12 mg/lb. A fourth group was given saline solution as a control. Each patient received a ketamine anesthetic in standard surgical dosages. This group of investigators found that droperidol had no significant influence on such side effects of ketamine as muscle rigidity, hypertension, and tachycardia. However, hallucinations, nausea, and vomiting were significantly lower in the droperidol groups and the higher dosages of droperidol reduced "bad" or unpleasant dreaming by more than half.

For dental out-patient applications, nitrous oxide-oxygen analgesia is usually administered by a nose mask at concentrations of 20-50 per cent.[39,40,41] Following administration of moderate amounts of nitrous oxide, there is a decreased acuity of pain.[39,40,41] The principal effect of nitrous oxide is analgesia and the analgesic potency increases in accordance with gas concentration.[40] It is commonly accepted that the action of the nitrous oxide in the blood stream is a purely physical one and that no chemical combination takes place with the tissues.[41,42] In their review of the literature, Hogue, Ternisky, and Iranpour noted that various other clinical observers had reported from 40 to 58.8 per cent incidences of nausea and vomiting with 40% nitrous oxide-oxygen concentration in administrations of over 30 minutes.[40] Therefore, we can assume that administration of nitrous-oxide enhances the possibility of vomiting during the procedure.

Although droperidol has been shown to reduce the incidence of vomiting and unpleasant psychic reactions, no studies evaluating either droperidol or nitrous oxide with ketamine for dental out-patient procedures have been reported. Several studies illustrate the cardiovascular

changes that occur under nitrous oxide administration.[39,40,42] These include an increase in oxygen level of the blood, a decrease in heart rate and output, and a decrease in arterial pressure. Everett and Allen[39] observed that these physiological responses are similar to those of a patient on oxygen alone.

Therefore, nitrous oxide used in combination with ketamine might be expected to enhance analgesia, provide a potential for nausea, and result in favorable cardiovascular responses.

METHODS AND MATERIALS

Sixty patients for this study were selected from out-patients at the Dental Clinic of the James Whitcomb Riley Hospital for Children in Indianapolis, Indiana. These patients were chosen to receive a general anesthetic for their dental treatment because they exhibited one or more of the following:

a. Severe apprehension and resistance in the emotionally disturbed child with multiple carious teeth after treatment with sedation had been attempted.
b. Mental retardation with inability to obtain minimal cooperation.
c. Significant physical handicaps such as cerebral palsy which prevented the patient from cooperating.
d. Multiple carious teeth in the very young preschool child who was non-communicative and uncooperative. Usual techniques of behavior management and sedation had been unsuccessful.

These patients ranged in age from 19 months to 23 years, with a mean age of 7.8 years. Each patient was randomly scheduled to receive one of three combinations of ketamine designated as either Treatment I, Treatment II, or Treatment III.

Treatment I	ketamine HCl	2 mg/lb
	scopolamine	.1-.3 mg
Treatment II	ketamine HCl	2 mg/lb
	scopolamine	.1-.3 mg
	droperidol	.025 mg/lb
Treatment III	ketamine HCl	2 mg/lb
	scopolamine	.1-.3 mg
	nitrous oxide-oxygen[a]	20-50%

[a] Figure 2.

Treatment I served as the control in this study and was the basis of comparison for the other groups, since ketamine and scopolamine were used consistently in each treatment. The dosage of ketamine was the same for each of the three groups (2 mg/lb). Scopolamine was given as a mixture with ketamine in the same syringe by an intramuscular (IM) injection in the patient's lateral thigh. Scopolamine was chosen for antisialagogue and minor hypnotic effects, as recommended by previous mentioned reports.[1,6,9,20,43] Droperidol was administered IM in Treatment II in the lateral thigh musculature immediately after ketamine and scopolamine. A tuberculin syringe (1 cc) was generally useful to inject the small quantities of droperidol necessary (.1-1.0cc).

In Treatment III, nitrous oxide was administered after the start of anesthesia with ketamine using a semiclosed apparatus with a nose mask (Figure 2). The gaseous ratio of nitrous oxide-oxygen was dependent on the need to maintain the patient in a quiet state. A more resistive patient received a maximum of 50 per cent nitrous oxide until more relaxation resulted. Afterward the level of nitrous oxide was reduced.

After a medical history ruled out a history of cerebral vascular accident or uncontrolled grand mal seizures,[1,7] the child's parents were instructed not to give the child any food after six hours before the dental appointment (Instructions for Parents Concerning Sedation, Exhibit #1 in Appendix). This precaution minimized the possibility of nausea and vomiting during anesthesia. The parents were also informed that the child would receive the general anesthetic by injection in the leg and after the dental treatment they would be asked to stay with him until he was able to return home.

A pilot study including over fifty pedodontic patients was completed to determine the minimum dosage of ketamine to be administered IM for at least 30 minutes of anesthesia working time. Dosages

less than 2 mg/lb were found unsatisfactory to produce this desired period of anesthesia consistently; therefore, 2 mg/lb of ketamine IM was maintained during the controlled portion of the study. According to the manufacturer,[1] the accepted IM dose for surgical procedures is in the range of 4-6 mg/lb; consequently, the amount of anesthetic administered was still far below the usual accepted dosage. Since ketamine in low dosages does not usually produce surgical anesthesia, a local anesthetic, Xylocaine® (2% solution with 1:100,000 epinephrine), was also administered in the area of treatment.

The working time was measured from the time when the first injection was administered until the procedure was completed or a second injection was necessary. Additional injections were given when the patient began movements which made restorative dentistry difficult (the beginning of emergence).

Pre and Post Treatment

The mental status of each patient was evaluated as he entered the dental clinic treatment room by the same investigator (the author). The patient was classified as normal, slow or retarded according to the following criteria:

1. Normal--a child presently attending school and in the expected grade level for his age or a preschool child with a history of no learning disabilities and normal speech.
2. Slow--- a child presently attending special education classes for educable or trainable rated intelligence. A child who demonstrates ability to dress himself or become toilet-trained.
3. Retarded- a child classified as mentally retarded by a physician or special educator who fails to

demonstrate even minimal comprehension or cooperation in a dental chair.

In addition to the preassessment of the patient's mental status, he was evaluated preoperatively according to a consistent series of physical and mental tasks and given a score according to the following objective criteria (Physical and Mental Measurement Form, Exhibit #2, in Appendix).

1. a. Motor coordination and gait (3 points):
   Good - essentially normal, able to walk well unaided.
   Fair - some disability, able to walk but somewhat unsteady.
   Poor - marked disability, unable to walk without aid.
   Unsatisfactory - unable to walk even with aid.

   b. Entry to chair (3 points):
   same criteria as above

2. Memory score (5 points):
   The patient is asked to identify items in a series of five colorful pictures with easily recognizable objects including an automobile, horse, bird, Indian, and rabbit.

3. Finger-finger and finger-nose test (4 points):
   The subject's coordination is measured by asking him to touch two index fingers of each hand together and to touch the nose with eyes open and closed.

4. Response to commands (3 points):
   The patient is asked to hold up his hand, open his mouth, or close his eyes.

5. Color discrimination (3 points):
   The patient identifies three different color panels, red, blue and yellow.

6. Counting procedure (3 points):

The patient determines how many fingers the evaluator is holding up.

The total number of points for complete performance of the physical and mental measurements is 24. The mean scores of the preoperative mental and physical evaluation tests were as follows:

1.	Normal	15.8
2.	Slow	10.0
3.	Retarded	4.1

Following dental treatment and during recovery, the same investigator evaluated the physical and mental abilities of the patient at 30-minute intervals. The motor coordination and gait (Item 1) was the most reliable measurement to compare patients with differing test scores. This item was always the last measurement which the patient could perform satisfactorily. When the patient was able to equal his preoperative score, he was judged fully recovered from the anesthesia and discharged to the parent's care.

Operating Procedure

After preoperative tests were completed, the anesthetic in Treatment I, II or III was administered IM. The time required for the onset of anesthesia was recorded. The arrival of the anesthesia was identified by a fixed stare and catalepsy.[a] The local anesthetic was given according to the usual methods of local nerve blockage for dental procedures within accepted dosages.[b] All restorative treatment was performed by pedodontic interns, residents or faculty. A rubber dam was used to prevent aspiration of foreign particles and to minimize stimulation of the posterior wall of the pharynx. A mouth prop was generally necessary as some rigidity of the masticatory

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[a] Figure 5.
[b] Figure 6.

muscles was usually present.[a]

In the event of any complication during anesthesia, complete resuscitation equipment was available including positive ventilation oxygen (Figure 3), airways and orotracheal tubes, laryngoscope, intravenous catheters, and emergency drugs such as epinephrine and succinylcholine. The clinic dentists and auxiliaries were instructed on how to summon assistance for such emergencies as laryngospasm or cardiac arrest. An Indiana University staff anesthesiologist was immediately available if a serious emergency developed.

The restorative procedures were usually limited to 90 minutes. Afterward, the patient was moved to a darkened recovery room to stay with the parent until dismissal (Figure 4). Previously the parents had been given written instructions not to stimulate the child verbally or tactilely during recovery to avoid emergence reactions. All procedures were documented by the same investigator, including medical status of the patient, pulse and respiration, course of the anesthetic, drug dosages, treatment and recovery time, and side effects or complications (Ketamine Evaluation Form, Exhibit #3, in Appendix). The operator was asked to give his clinical impression of the quality of the anesthesia. If the patient was quiet or relatively quiet throughout the procedure, he rated the anesthetic excellent; if the patient moved but adequate restorative dentistry could be performed, he considered the anesthesia good. A rating of fair indicated improvement in behavior but some difficulty was encountered. The operator rated the anesthetic poor if some serious problems were encountered making the anesthetic unsatisfactory.

The parents were given a questionnaire form and instructions to complete it relative to the patient's travel home and for the first 24 hours following dismissal from the clinic (Sedation Questionnaire Form, Exhibit #4 in Appendix). The form was to be returned to the

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[a] Figure 7.

James Whitcomb Riley Hospital Dental Clinic in a self-addressed, stamped envelope.

RESULTS

A statistical analysis was performed on the data obtained for the three treatments to measure significant differences in Treatment I, II or III on the basis of working time and recovery time. In addition, the relationship of intelligence, as measured by the patient's test scores, to working time and recovery time in each of the three treatments was examined.

Using analysis of variance, significant differences were found when comparing test scores and working times between the various groups but not for recovery times. Further "t" tests using the Newman-Keuls method recorded significantly longer working time and higher intelligence in Treatment III, whereas recovery and working times as well as intelligence were not significantly different in other treatments.

The results of each anesthetic case are recorded in Table I including the number of injections of ketamine, working time under the anesthetic, recovery time, and the patient's test score. The mean working and recovery times are recorded in Table II according to treatment and according to intelligence.

Table III is a summary of statistically significant values as measured at the .05 level of confidence. Working time, recovery time, and test scores are compared according to treatment and intelligence. Tables IV-XII include a detailed statistical analysis of all three variables using analysis of variance and Newman-Keuls "t" tests.

A mixture of ketamine and scopolamine, or ketamine, scopolamine, and droperidol was used initially, but all subsequent injections used ketamine alone. The time of onset of anesthesia from the first injection ranged from 3-7 minutes with an average of 5 minutes in all three groups. The total number of injections necessary to provide satisfactory anesthesia in 60 minutes of working time was recorded. A linear relationship was found in comparing the number of injections

with intelligence. Whereas the dental procedures for 50 per cent of the normal group were completed with one injection, 56 per cent of the slow group and 73 per cent of the retarded children were completed with only one injection (Table XIII). In Table XIV, a marked decrease in the number of repeat injections necessary was found in Treatment III vs. Treatments I and II.

The incidence of complications was recorded according to treatment and intelligence: normal, slow, and retarded (Table XV). Only one child vomited during the anesthetic. This incidence caused no particular difficulty as the patients' normal laryngeal reflexes were present and the anesthetic was administered on an empty stomach. The single incident of a parent reporting her son hallucinating occurred in a 23-year-old retarded patient weighing 179 pounds. Although the recovery period was uneventful, the mother later responded with dissatisfaction due to difficulty in handling her irritable son during the post-emergence period.

A blockage of the airway was encountered with three Down's Syndrome patients in both Treatments I and II. All three patients exhibited macroglossia and relative prognathism characteristic of this syndrome. A single incident of a partial lagyngospasm was recorded in a 12-year-old normal female. The patient reported a history of a recent common cold but exhibited no nasal congestion and was afebrile at the time of anesthesia. The patient was resuscitated immediately with no difficulty using positive oxygen ventilation alone. No pattern of complication compared to treatment or intelligence was observed.

The operator's responses to each of the three combinations of ketamine were consistently high, with most operators reporting excellent or good anesthesia (Table XVI).

Among the questions on the Sedation Questionnaire Form (Appendix #4) were these: "Did you have any difficulty managing your child after you got home?" and "Do you feel that this method of sedation was favorable or unfavorable for your child's dental treatment?" With 80 per cent of the questionnaires returned, 85 per cent of the parents responded favorably, 12 per cent unfavorably, and 3 per cent were unsure (Table XVII). No large difference in favorable or unfavorable response was noted from parents according to which treatment the child received.

ILLUSTRATIONS

Figure 1. Commercial preparations of the injectable agents used in the study: droperidol, scopolamine, and ketamine.

Figure 2. Chemetron nitrous oxide-oxygen analgesia apparatus used in the study. This machine, manufactured by National Cylinder Gas, is semiclosed and uses a nose mask.


KETALAR
50 MG. PER ML.
PARKE-DAVIS

Figure 3. Puritan positive pressure oxygen apparatus used for emergency resuscitation.

Figure 4. Recovery facility used for patients during the recovery period. This area should be kept dark and quiet to avoid unpleasant reactions by the patients.

Figure 5. Patient anesthetized with ketamine. This patient demonstrates clinical signs of catalepsy and aimless staring characteristic of ketamine anesthesia.

Figure 6. Local anesthetic being administered to patient anesthetized with ketamine. Masticatory muscles are rigid necessitating the use of a mouth prop.

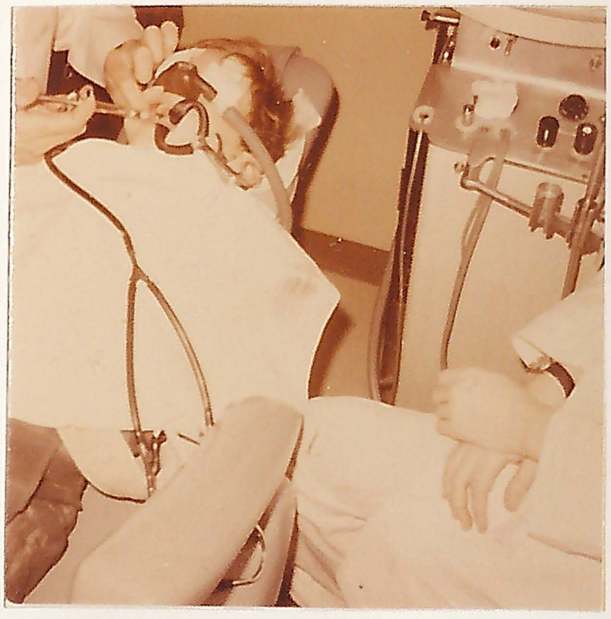


Figure 7. Anesthetized patient ready for restorative dentistry. Nitrous oxide nose mask, rubber dam, and mouth prop are in place. Cotton gauze squares are placed over the eyes to avoid debris and light stimulation.

TABLES

Table I

Raw Data on Number of Injections, Working Time, Recovery Time, and Test Scores

First figure - number of injections of ketamine HCl
Second Figure - working time under anesthetic
Third figure - recovery time from last injection
Fourth figure - patient test score

Normal	Slow	Retarded
	Treatment I	
1, 60, 195, 11	2, 35, 93, 6	2, 20, 105, 2
2, 14, 138, 6	1, 60, 88, 8	1, 60, 150, 6
2, 60, 120, 15	1, 50, 105, 4	1, 60, 135, 4
2, 11, 128, 14	1, 40, 120, 4	1, 30, 75, 0
	1, 70, 204, 6	1, 30, 127, 0
		2, 37, 150, 2
		3, 27, 150, 4
		3, 48, 150, 4
		1, 60, 150, 4
		1, 60, 158, 4
		2, 11, 152, 6
	Treatment II	
1, 60+, 90, 6	2, 52, 145, 0	2, 25, 95, 0
2, 30, 126, 24	3, 30, 105, 6	1, 40, 146, 0
2, 20, 155, 6	3, 15, 95, 6	1, 60, 195, 2
2, 30, 128, 24	2, 60, 137, 6	1, 80, 169, 6
1, 60, 192, 13	1, 40, 135, 24	1, 60, 130, 2
	2, 60, 145, 6	1, 25, 130, 6
		2, 35, 180, 0
		1, 40, 122, 6
		2, 0, 240, 6

Table I (continued)

Raw Data on Number of Injections, Working Time, Recovery Time, and Test Scores

First figure - number of injections of ketamine HCl
Second figure - working time under anesthetic
Third figure - recovery time from last injection
Fourth figure - patient test score

Normal	Slow	Retarded
	Treatment III	
1, 60+, 160, 24	3, 24, 155, 22	1, 90, 135, 6
1, 80, 120, 24	1, 60+, 143, 18	1, 60+, 132, 12
1, 60+, 210, 24	1, 60+, 135, 6	1, 60+, 132, 6
2, 60+, 115, 6	1, 60+, 86, 4	1, 40, 200, 6
1, 60+, 150, 24	1, 60+, 120, 24	1, 60+, 155, 6
	1, 60+, 124, 6	1, 60+, 96, 2
	1, 60+, 240, 24	1, 60+, 128, 6
		1, 60+, 155, 2

Table II

Means of Working Time and Recovery Time Across Treatments and Intelligence Levels

Mean	Normal		Slow		Retarded	
	W.T. (Min.)	R.T. (Min.)	W.T. (Min.)	R.T. (Min.)	W.T. (Min.)	R.T. (Min.)
Treatment I	36.25	145.25	51.00	122.00	40.27	136.55
Treatment II	40.00	138.20	42.83	127.00	40.55	156.22
Treatment III	64.00+	151.00	54.86+	143.28	61.25+	141.63
Average	47.50+	142.64	49.78+	131.94	47.27+	146.87

Average	Working Time	Recovery Time
Treatment I	42.15 min.	134.65 min.
Treatment II	41.10 min.	143.00 min.
Treatment III	59.70+ min.	144.55 min.

Table III

Summary of Significant Differences in Working Time, Recovery Time, and Test Scores Across Treatments and Intelligence Levels

	I - II	I - III	II - III
		Treatment	
Working Time	N.S.D.	*	*
Recovery Time	N.S.D.	N.S.D.	N.S.D.
Test Score	N.S.D.	*	*
		Intelligence Level	
	Norm-Slow	Norm-Retard	Slow-Retard
Working Time	N.S.D.	N.S.D.	N.S.D.
Recovery Time	N.S.D.	N.S.D.	N.S.D.
Test Score	*	*	*

* Significant difference measured at .05 level.

Table IV

Working Time Means, Standard Deviations, and Analysis of Variance Across Both Treatments and Intelligence Levels

Cell	No. of Reps.	Mean Y	Std. Dev. Y
1N	4	36.25000	27.45147
2S	5	51.00000	14.31782
3R	11	40.27273	18.11679
4N	5	40.00000	18.70829
5S	6	42.83333	18.00463
6R	9	40.55556	23.64377
7N	5	64.00000	8.94427
8S	7	54.85714	13.60672
9R	8	61.25000	13.56203

Analysis of Variance Table

Source	Sum of Squares	D.F.	Mean Square	F
Mean	124972.53	1	124972.53	384.54608
Treatments	4157.5759	2	2087.7879	6.42422*
Intelligence NSR	75.198416	2	37.599208	.11569 NSD
Interaction	837.72839	4	209.43210	.64443 NSD
Error	16574.345	51	324.98715	

* Significance measured at .05 level.

Table V

Working Time Mean, Standard Deviation, and Neuman-Keuls "t" Tests For Significant Difference Across Treatments

Group	Count	Mean	Standard Deviation
Treatment I	20	42.1500	19.1016
Treatment II	20	41.1000	19.8942
Treatment III	20	59.7000	12.5535
Total	60	47.6500	19.2282
Subset 1			
Group	Group 2	Group 1	
Mean	41.1000	42.1500	
Subset 2			
Group	Group 3		
Mean	59.700		

* Significance measured at .05 level.

Group 1 vs Group 2: N.S.D.
Group 1 vs Group 3: *
Group 2 vs Group 3:*

Table VI

Working Time Means, Standard Deviation, and Newman-Keuls "t" Tests for Significant Differences Across Intelligence Levels

Group	Count	Mean	Standard Deviation
Normal	14	47.5000	21.7141
Slow	18	49.7778	15.3950
Retarded	28	46.3571	20.6617
Total	60	47.6500	19.2282

Subset 1

Group	Norm	Slow	Retard
Mean	47.5000	49.7778	46.3571

Group 1 vs Group 2: N.S.D.
Group 1 vs Group 3: N.S.D.
Group 2 vs Group 3: N.S.D.

No significant differences were found.

Table VII

Recovery Time Means, Standard Deviations, and Analysis of Variance Across Both Treatments and Intelligence Levels

Cell	No. of Reps.	Mean	Standard Deviation
1	4	145.25000	33.97425
2	5	122.00000	47.47104
3	11	136.54545	25.45727
4	5	138.20000	37.92361
5	6	127.00000	21.54066
6	9	156.33333	44.22952
7	5	151.00000	38.14446
8	7	143.28571	47.88080
9	8	141.62500	29.90909

Analysis of Variance Table

Source	Sum of Squares	D.F.	Mean Square	F	
Mean	1070082.7	1	1070082.7	796.4995	
Treatment	1022.7945	2	511.39724	.38065	N.S.D.
Intelligence	2449.2933	2	1224.6467	.91155	N.S.D.
Interaction	2562.7396	4	640.68491	.47688	N.S.D.
Error	68517.581	51	1343.4820		

Significance measured at .05 level.

Table VIII

Recovery Time Mean, Standard Deviation, and Neuman-Keuls "t" Tests for Significant Differences Across Treatments

Group	Count	Mean	Standard Deviation
Treatment I	20	134.6500	32.6437
Treatment II	20	143.0000	37.6787
Treatment III	20	144.5500	37.0810
Total	60	140.7333	35.5298

Subset 1 Group	T-1	T-2	T-3	
Mean	134.6500	143.0000	144.5500	N.S.D.

No significant differences were found.

Group 1 vs Group 2: N.S.D.
Group 1 vs Group 3: N.S.D.
Group 2 vs Group 3: N.S.D.

Table IX

Recovery Time Means, Standard Deviation and Neuman-Keuls "t" Tests for Significant Differences Across Intelligence Levels

Group	Count	Mean	Standard Deviation
Normal	14	144.7857	34.4700
Slow	18	131.9444	39.5794
Retarded	28	144.3571	33.5628
Total	60	140.7333	35.5298

Subset 1

Group	Normal	Slow	Retarded
Mean	131.9444	144.3571	144.7857

No significant differences were found.

Group 1 vs Group 2: N.S.D.
Group 1 vs Group 3: N.S.D.
Group 2 vs Group 3: N.S.D.

Table X

Test Score Means, Standard Deviation, and Analysis of Variance Across Both Treatments and Intelligence Levels

	Cell	No. of Reps.	Mean	Standard Deviation
Treatment I	1	4N	11.5	4.0
	2	5S	5.6	1.6
	3	11R	3.8	1.8
Treatment II	4	5N	14.6	9.0
	5	6S	8.0	8.1
	6	9R	3.1	2.8
Treatment III	7	5N	20.4	8.0
	8	7S	14.8	9.1
	9	8R	5.7	3.1

Analysis of Variance Table

Source	Sum of Squares	D.F.	Mean Square	F
Mean	80.5	1	80.5	2.5
Treatment	378.0	2	189.0	5.9*
Intelligence	1218.5	2	609.2	19.1*
Interaction	112.3	4	28.0	.8 N.S.D.
Error	1555.7	49	31.7	

* Significance measured at .05 level.

Table XI

Test Score Mean, Standard Deviation, and Neuman-Keuls "t" Tests For Significant Differences Across Treatments

Group	Count	Mean	Standard Deviation
Treatment II	20	5.8000	3.7641
Treatment I	20	7.4500	7.7966
Treatment III	20	12.6000	9.0169
Total	60	8.6167	7.6714

Subset 1

Group	Treatment II	Treatment I
Mean	5.8000	7.4500

Subset 2

Group	Treatment III
Mean	12.6000

* Significance measured at .05 level.

Group 1 vs Group 2: N.S.D.
Group 1 vs Group 3: *
Group 2 vs Group 3: *

Table XII

Test Score Means, Standard Deviation, and Neuman-Keuls "t" Tests for Significant Differences Across Intelligence Levels

Group	Count	Mean	Standard Deviation
Normal	14	15.7857	7.9535
Slow	18	10.0000	8.1746
Retarded	28	4.1429	2.7178
Total	60	8.6167	7.6714

Subset 3		Subset 2	
Group	Normal	Group	Slow
Mean	15.7857	Mean	10.0000

Subset 1	
Group	Retarded
Mean	4.1429

* Significance measured at .05 level.

Group 1 vs Group 2: *
Group 1 vs Group 3: *
Group 2 vs Group 3: *

Table XIII

Number of Injections Received in Each Treatment Group Across Intelligence Levels

First Column - number of patients receiving one injection.
Second Column - number of patients receiving two injections.
Third Column - number of patients receiving three injections.

	Normal	Slow	Retarded
Treatment I	1, 3 (25%, 75%)	4, 1 (80%, 20%)	6, 3, 2 (55%, 27%, 18%)
Treatment II	2, 3 (40%, 60%)	1, 3, 2 (17%, 50%, 33%)	6, 3 (67%, 33%)
Treatment III	4, 1 (80%, 20%)	4, 0, 1 (80%, 0%, 20%)	10, 0 (100%, 0%)
Total	7, 7 (50%, 50%)	9, 4, 3(56%, 25%, 19%)	22, 6, 2(73%, 20%, 7%)

Parenthesis - above figures translated to percentages.

Table XIV

Patients Requiring More than One Injection of Ketamine Across Treatments and Intelligence Levels

	Normal	Slow	Retarded	
Treatment I	3	1	5	9/20 (45%)
Treatment II	3	5	3	11/20 (55%)
Treatment III	1	1	0	2/20 (10%)
	7/14 (50.0%)	7/18 (38.9%)	8/28 (28.6%)	

Table XV

Complications Noted Across Treatments and Intelligence Levels

	T-1	T-2	T-3
Vomiting	0, 0, 0	0, 0, 0	0, 0, 1
Hallucinations	0, 0, 0	0, 0, 0	0, 0, 1
Tongue blocking airway	0, 0, 2	0, 1, 0	0, 0, 0
Other airway obstruction	0, 0, 0	0, 0, 0	1, 0, 0
	2	1	3

Column 1 are normal, column 2 slow, column 3 retarded under each treatment.

Total number of complications by intelligence level:

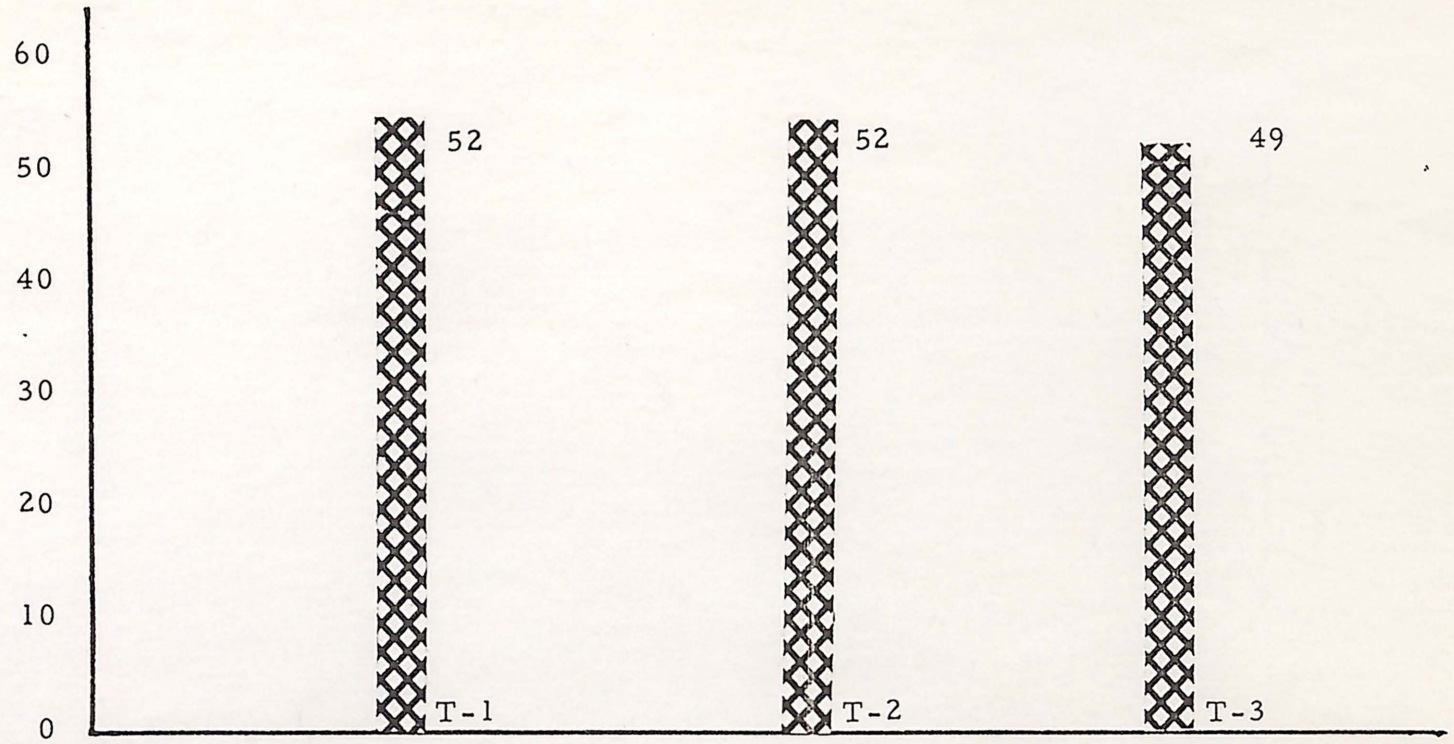
Normal 1

Slow 1

Retarded 4

Table XVI

Quality of Anesthesia as Judged by Operator Across Treatments



Total number for each treatment indicates the sum of the responses of the operators for the 20 patients in each group based on the following rating scale:

Excellent, 3; Good, 2; Fair, 1; and Poor, 0.

Table XVII

Record of Unfavorable Responses of Parents to Anesthetic Across Treatments and Intelligence Levels

	T-1	T-2	T-3
Difficulty managing child	0, 0, 2	0, 0, 0	1, 1, 1
Unfavorable to this method of anesthesia	0, 0, 0	1, 0, 0	0, 0, 1
Unfavorable response	2/20	1/20	4/20

Column 1 are normal, Column 2 slow, Column 3 retarded under each treatment.

Total number of unfavorable responses by intelligence levels:

Normal 3/60

Slow 1/60

Retarded 4/60

(Response percentages were: favorable 85%; unfavorable, 12%, unsure, 3%.

One unsure response was recorded by the retarded in Treatment II and the normal in Treatment III.

DISCUSSION

In adapting the general anesthetic agent, ketamine, to pedodontic out-patients, the main objective was to develop a method of administration which would provide safe, profound anesthesia with little or no unpleasant side effects and a short recovery period. Although ketamine was shown in other studies to provide effective and safe anesthesia for short surgical or diagnostic procedures, many reports demonstrated long recovery times and a significant incidence of hallucinations and unpleasant emergence reactions in adults.[6, 11, 12, 18, 33] Accordingly, the three methods of administering ketamine in Treatments I, II and III were designed to eliminate as many undesirable side effects as possible. A small dosage of ketamine was administered in each treatment, sufficient to take the patient to a light stage of anesthesia. Local anesthetic was necessary to avoid awakening the patient with a painful stimulus.

Length of Anesthesia

The working time, or the length of anesthesia sufficient to allow the operator to provide careful, restorative dentistry with one injection of ketamine at 2 mg/lb IM, averaged 41.10 to 59.70 + minutes (Table II). This length of time was sufficient to complete from 45% (Treatment II) to 90% (Treatment II) of the operative procedures without additional anesthetic. Although Treatments I and II compared very closely in length of working time, Treatment III required far fewer second injections. As a result, the performance of Treatment III was considered better in this respect.

When the working times were compared across intelligence levels, no correlation could be found between any treatment and a longer or shorter working time. In an earlier pilot study using ketamine at 1 mg/lb, some success was found in sedating normal children. However, ketamine at this dosage failed to provide

consistent anesthesia in mentally handicapped or very young patients. As a result the dosage was increased to 2 mg/lb to provide consistent anesthesia in all groups of children.

The working times of Treatment III are designated with a plus (+) to indicate that the actual working time would have been longer if the nitrous oxide analgesia had not been discontinued. Treatments I and II showed comparable average working times of 42.15 and 41.0 minutes. However, Treatment III demonstrated average working times of over 59.70 minutes. We can expect that if nitrous-oxide analgesia had been continued after the end of the procedures, significantly higher working times could be demonstrated than are shown here.

Recovery Period

Other studies have defined the recovery period as the time from the last injection of ketamine.[6, 12, 18, 19] Using that basis in this study, the recovery times compare very closely to one another measured across treatments or intelligence levels (Table II). Treatment I recorded the lowest average recovery time of 134.65 minutes, whereas Treatments II and III compare very closely at 143.00 and 144.55 minutes. However, these values do not seem to reflect themselves clinically as Treatment III consistently required few additional doses of ketamine. Therefore, if the length of time is recorded from the first injection of ketamine until the patient is fully recovered, regardless of the number of repeat injections, the following average recovery times are noted: Treatment I - 151.60 minutes, Treatment II - 156.60 minutes, Treatment III - 150.30 minutes. Although these figures reflect more accurately the clinical picture, analysis shows that they are not statistically different due to the similarity of the means and to the wide variance of recovery times.

Intelligence Level

When the mental and physical pre-anesthetic test was developed, it was expected that a correlation might be shown between the degree of mental disability and the dosage of ketamine necessary or the length of working and recovery time. Insignificant differences were detected in both working times and recovery times measured across intelligence levels. However, an interesting linear relationship did occur among patients in all three treatments requiring more than one injection of ketamine (Table XIV). Children showing a greater degree of mental disability tended to require additional injections less frequently. Additional injections of ketamine were given at a dosage of 1 mg/lb instead of 2 mg/lb. Since recovery time was measured from the time of the last injection, repeat injections of a lower dosage would tend to require shorter recovery periods. As the number of injections does not seem to increase the length of recovery time and later dosages are smaller, the differences in the length of recovery measured across intelligence may have been greater than the results suggest. The test scores correlated well with the three intelligence groupings as used in this study, with a mean of 4.1 for the retarded group, 10.0 for the slow group, and 15.8 for the normal group (Table XII). These values demonstrated statistical significance using Newman-Keuls "t" tests.

If the patients were chosen randomly we should expect no significant differences in test scores measured across treatments. Although Treatments I and II show comparable test scores between groups, Treatment III shows a significantly higher ($p<.05$) group mean. Therefore, the mental status or at least the cooperation for testing may have been slightly higher in Treatment Group III. Perhaps

this discrepancy can be explained by the problem of frequent nasal congestion and the difficulty in fitting a nitrous-oxide nose mask on a small child. Therefore, these patients who tended to score very low on the preoperative test seemed to be selected out of the group for Treatment III.

Complications

Any undesirable side effects of anesthesia in Treatments I, II or III were recorded on the Ketamine Evaluation Form (Exhibit #3 in Appendix). Only complications that occurred during anesthesia or the recovery period were generally noted. The exception was made for hallucinations as this was considered a sufficiently serious problem in other studies of adults to warrant careful evaluation in this investigation.

Vomiting was a potential concern as aspiration of debris into the lungs can be demonstrated during ketamine anesthesia.[31] It was expected that by reducing the dosage from 1/2 to 1/3 that used in surgical procedures,[6, 9, 44] this complication could be further reduced. In the pilot study, vomiting had been somewhat of a problem (9 per cent) with no attempt made to restrict the intake of food. During the present investigation, all parents were given specific instructions to avoid giving the patient food six hours before the anesthetic. This precaution dramatically reduced the incidence of vomiting, and if regurgitation did occur the amount of vomitus was small.

A mechanical obstruction by the the tongue occurred in three instances in Treatment II, involving in all cases Down's Syndrome children. It is the author's opinion that this complication was related more to the unusual anatomy of the lower face and oral cavity of this type of child than to the method of treatment. Caution should be

exercised by anyone planning an anesthetic procedure on a Down's child without intubation. It was noted that during the obstruction period in these patients, a clear airway could be maintained by elevating the jaw or returning the patient to an upright sitting position.

The ease of administration and consistent good results of ketamine anesthesia tend to give the anasthetist a false sense of security. On occasion a laryngospasm can occur with serious results.[6, 9] Consequently, ketamine should not be administered by someone untrained in anesthesia principles and resuscitory procedures. In Treatment III, a single event of partial laryngospasm occurred in a healthy, normal 12-year-old female. The problem was relieved by administering 100 per cent oxygen with a positive pressure apparatus. The low incidence of hallucinations noted in this investigation was recorded over a 24-hour period using a Parent's Evaluation Form (Exhibit #4 in Appendix). In previous studies, other investigators have reported fewer unpleasant emergence or post-recovery psychic reactions in children given IM doses of ketamine.[9, 17, 33] The overall results of this study are in agreement here; the exception was a 23-year-old, 179 pound retarded patient. He was described by the parent as "reaching for things that weren't there" during the post recovery period. The hallucinations did not continue the next day and no other ill effects were noted.

Operator and Parent Response to Anesthesia

The quality of anesthesia as judged by the operator was a matter of personal opinion. The operators consisted of clinical pedodontists with a background in treating handicapped children with and without sedation or anesthesia. If the patient was reasonably quiet

during the working period, the operators tended to be well satisfied with the method of anesthesia (Table XVI). In most cases all three treatments received either good or excellent appraisals by the pedodontists. No attempt was made to do a blind study regarding the particular treatment being used, as this would have been impractical considering the obvious nature of each form of treatment.

The clinical pedodontists who participated in the investigation rated ketamine anesthesia high in comparison to other sedatives and hypnotics used in treating handicapped children. The main criticism of ketamine found in all three treatments was the length of recovery time. However, as the study progressed, it was noted that a certain amount of anesthetic inertia remained beyond the actual working period and if the procedure was near completion, reasonable co-operation could be obtained by restraint instead of additional injections of ketamine. Fewer total injections of ketamine helped to shorten the time until the patient was discharged. During the latter period of anesthesia, the patient began to exhibit purposeless movements and unintelligible sounds. Analgesia and amnesia continued until well into the recovery period.

The parents were invited to comment favorably or unfavorably on this method of sedation. No attempt was made to select out parents who regarded any form of sedation unfavorably. Most parents had seen their child at one time or another premedicated for dental treatment, but for others the treatment with ketamine was their first experience with an anesthetic drug. Twelve per cent responded unfavorably, 85 per cent favorably, and 3 per cent were unsure. Considering the alternative of treatment with a hospital admission and a conventional gaseous anesthetic, these percentages were considered very satisfactory.

SUMMARY AND CONCLUSIONS

An eleven-month study has compared the clinical performance of three methods of administering ketamine HCl in pedodontic out-patients. Sixty behavior problem children were given ketamine and scopolamine (Treatment I), ketamine, scopolamine, and droperidol (Treatment II), or ketamine, scopolamine and nitrous oxide-oxygen analgesia (Treatment III) for restorative dental procedures. Each treatment group contained twenty randomly selected children. The treatments were administered by a uniform method and dental procedures of 60-90 minutes were completed. The length of effective anesthesia from the initial injection was measured and the length of recovery time from the last injection of ketamine (IM) was recorded. The patient was discharged when he was able to achieve the same score that he had achieved preoperatively on a series of mental and physical tests. Comparisons were made across treatments and intelligence levels (normal, slow, retarded) of the working time, recovery time, incidence of complications, and operator and parent response.

Treatment III (ketamine, scopolamine, and nitrous oxide) produced the longest working time as well as the shortest recovery time. Treatments I and II produced shorter working times and longer recovery times. The incidence of complications and the quality of anesthesia as judged by the operator were very similar in all three treatments. The percentage of favorable responses to this form of anesthesia was comparably high in all three methods of treatment.

Safe, effective anesthesia can be provided for behavior problem pedodontic out-patients using ketamine IM providing the following procedures are used:

1. Ketamine is administered in a dosage of 2 mg/lb together with scopolamine .1 - .3 mg. Nitrous oxide may be used to supplement ketamine to lengthen working time.

2. Outside stimulation including light, tactile, or verbal should be reduced to a minimum. Local anesthetic should be employed.
3. The patient should be on a fasting diet prior to anesthesia and the medical history should rule out a history of severe uncontrolled seizures or cerebrovascular accident. A patient who presents with respiratory congestion or a cold should be rescheduled for a later time.
4. All operative procedures should be completed using a rubber dam to minimize aspiration of debris and unnecessary stimulation of the posterior pharyngx.
5. To minimize the possibility of hallucinations, ketamine anesthesia should be limited to children.
6. Ketamine is best suited to short operative procedures (<90 minutes) and should be administered only by operators with anesthesia training.

APPENDIX

Forms Used for Ketamine Anesthetic Procedure

Exhibit #1

INSTRUCTIONS FOR PARENTS CONCERNING SEDATION

At your child's next appointment he will be given sedation to gain his cooperation and to enable his doctor to complete the dental treatment. In order to make his appointment as comfortable as possible, please observe the following recommendations.

1. If your child's appointment is in the morning, please restrict the diet to clear fluids for breakfast such as apple juice or soda. For an afternoon appointment, give no solid foods for six hours before the appointment time. This will help prevent nausea experienced by some children.

2. Be sure your child gets a good nights sleep before his appointment.

3. After the appointment, your child will be awake but drowsy. Let him remain as quiet as possible. Loud talking, shaking, or other means to get your child's attention may only confuse him initially. If you have a long car ride ahead of you, your doctor may request that you remain until he feels your child is sufficiently awake to travel. Your child may wish to sleep on and off for several hours or until the morning after his appointment.

4. It is important that you complete the recovery evaluation form which will be given to you on the day of your appointment in order to evaluate your child's experience for future appointments.

Riley Dental Clinic

Exhibit #2

Physical and Mental Measurement Form

. Motor Coordination
a) Gait GFPV
b) Entry to chair GFPV

. Memory Score

1 2 3 4 5

. Finger-finger-test +-±
Finger-nose + - ±

. Able to respond to simple commands
a) Hold up hand
b) Open mouth
c) Close eyes

. Color discrimination
Red Green Black

. Number of fingers
a) three
b) one
c) two

1. Motor Coordination
a) Gait GFPV
b) Exit fromchair GFPV

2. Memory Score

1 2 3 4 5

3. Finger-finger + - ±
Finger-nose + - ±

4. Able to respond to simple commands
a) Hold up hand
b) Open mouth
c) Close eyes

5. Color Discrimination
Red Green Black

6. Number of fingers
a) three
b) one
c) two

1. Motor Coordination
a) Gait GFPV
b) Entry from chair GFPV

2. Memory Score

1 2 3 4 5

3. Finger-finger + - ±
Finger-nose + - ±

4. Able to respond to simple commands
a) Hold up hand
b) Open mouth
c) Close eyes

5. Color Discrimination
Red Green Black

6. Number of fingers
a) three
b) one
c) two

1. Motor Coordination
a) Gait GFPV
b) Exit from chair GFPV

2. Memory Score

1 2 3 4 5

3. Finger-finger + - ±
Finger-nose + - ±

4. Able to respond to simple commands
a) Hold up hand
b) Open mouth
c) Close eyes

5. Color Discrimination
Red Green Black

6. Number of fingers
a) three
b) one
c) two

Exhibit #3

Ketamine Evaluation Form

Code Number _____ (Please fill out completely) Date _____

Patient's Name; _____ Age___ Weight _____

Recent Medication:_____

Mental Status: a) normal b) slow c) retarded

Would the child cooperate for normal x-rays? YES NO

Initial Observation: a) cooperative b) apprehensive c) fearful
d) excited and uncooperative

	Before	During	After Procedure
Blood Pressure	_____	_____	_____
Pulse	_____	_____	_____
Respiration	_____	_____	_____

	Ketamine HCl	Scopolamine	Other
Induction Dose (time)	_____	_____	_____
Second Injection (time)	_____	_____	_____
Third Injection (time)	_____	_____	_____

What was onset time of anesthesia: _____ minutes

Maintenance:	Ketamine	Other
Second Injection (time)	_____	_____
Third Injection (time)	_____	_____

Course:	Quiet and Cooperative	Movement and Cooperative	Uncooperative
Local anesthesia	_____	_____	_____
Start of Procedure	_____	_____	_____
During Procedure	_____	_____	_____
Near end of procedure	_____	_____	_____
After the procedure	_____	_____	_____

Behavior deteriorated after first injection: 10 min__ 20min__ 30 min__
40 min__ 60 min__

Recovery:_____
_____

Complications: Facial Erythema _____ Dreaming_____
Nausea _____ Other (Specify) _____

Do you feel sufficient dosage was administered? YES NO

Description of procedure:_____

Anesthesia was: a) excellent b) good c) fair d) poor

RECOMMENDATIONS:_____

Exhibit #4
Sedation Questionnaire Form

Name_____
Date_____

Please complete the following questions and return the form immediately to Riley Dental Clinic. This is important in the future care of your child and becomes a part of his permanent medical record.

1. When you left the dental clinic was your child:
   a) asleep b) crying c) normal d) restless e) drowsy f) dreaming
2. On the way home, was your child:
   a) asleep b) awake but drowsy c) awake but restless d) dreaming
   e) about normal
3. Did your child vomit on the way home or after you arrived home?___
4. How long did it take to get home after leaving the clinic?_____
5. When you arrived home did your child walk into the house? YES NO
6. Did your child report any dreams: YES NO
   If so please describe _____
7. Did you have any difficulty managing your child after you got home?
   YES NO
8. Did your child want to sleep? YES NO
9. If your child slept, until what time did he (or she) sleep? _____o'clock
10. At what time did your child resume normal activities? _____o'clock
11. How did your child describe his dental experience? _____
    _____
12. Did you notice anything in your child's behavior that was unexpected?
    YES NO
    If so, please specify_____
    _____
13. Did your child have a temperature? YES NO
14. Do you feel that this method of sedation was favorable or unfavorable for your child's dental treatment?
15. Additional Comments: _____
    _____
    _____
    _____

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ABSTRACT

AN EVALUATION OF KETAMINE HYDROCHLORIDE IN PEDODONTIC OUTPATIENTS

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The need for a safe but effective agent to sedate dental patients who are severe behavior management problems prompted this investigation of ketamine HCl. Ketamine HCl is a general anesthetic agent with the unique property of selectively depressing the higher centers of the brain without adversely affecting respiration or cardiac output.

Sixty behavior problem pedodontic patients were selected at random and placed in one of three groups to receive the following treatments: Treatment I - ketamine HCl and scopolamine; Treatment II - ketamine, scopolamine, and droperidol, and Treatment III - ketamine, scopolamine, and nitrous oxide-oxygen analgesia.

Each treatment group received ketamine HCl 2 mg/lb and 0.1 - 0.3 mg scopolamine. The second two treatment groups were supplemented with droperidol .025 mg/lb or nitrous oxide-oxygen (20-50%) to maintain anesthesia.

The patients were given a series of pre and post-treatment mental and physical tests and were considered completely recovered when they could equal their pre treatment test scores. Routine dental restorative procedures limited to one and one-half hours were carried out with the use of the ruber dam.

Onset of anesthesia was five minutes for all three treatment groups. Treatment III showed a significantly longer working time but recovery times were not significantly different between groups. Ketamine HCl was determined to be a safe, effective agent for use in pedodontic outpatients provided prescribed techniques are followed. Complications were infrequent and minor and parental response was considered satisfactory.